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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte EVANGELOS KARAVAS,
KONSTANTINOS LIOUMIS, and STAVROS POLITIS

Appeal 2011-008002
Application 10/565,322
Technology Center 1600

Before TONI R. SCHEINER, DONALD E. ADAMS, and
STEPHEN WALSH, *Administrative Patent Judges*.

WALSH, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134(a) involving claims to a pharmaceutical dosage form comprising an extended release formulation of Venlafaxine HCL. The Patent Examiner rejected the claims as obvious. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

STATEMENT OF THE CASE

Claims 1-23 are on appeal. Claim 1 is representative and reads as follows:

1. A once a day pharmaceutical dosage form comprising an extended release formulation of the water-soluble drug substance Venlafaxine HCl, comprising a hard gelatin capsule containing a therapeutically effective number of mini tablets, wherein each mini-tablet comprises a functional core and a functional coating layer or a functional coating film, and wherein the functional core is produced with compression technology and comprises an extended release formulation of the water-soluble drug substance Venlafaxine HCl and wherein the functional coating layer or functional coating film coats the functional core and limits the initial rapid diffusion of the water-soluble drug substance from the functional core.

The Examiner rejected claims 1-23 under 35 U.S.C. § 103(a) as unpatentable over Sherman,[1] Oosterbaan,[2] and Mulye.[3]

Appellants have not raised separate arguments for claims 2-23, therefore these claims stand or fall with claim 1. 37 C.F.R. § 41.37(c)(1)(vii).

OBVIOUSNESS

The Issue

The Examiner's position is that Sherman taught a 24-hour extended release dosage formulation of Venlafaxine hydrochloride comprising starch

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[1] Patent No. US 6,419,958 B2 issued to Deborah M. Sherman et al., Jul. 16, 2002.
[2] Patent No. US 6,696,496 B2 issued to Marinus J. M. Oosterbaan et al., Feb. 24, 2004.
[3] Patent Application Publication No. US 2002/0155156 A1 by Nirmal Mulye, published Oct. 24, 2002.

or gelatin capsules containing film coated spheroids comprising a therapeutically effective amount of Venlafaxine hydrochloride. (Ans. 4-5.) The Examiner found that Sherman did not teach that its formulation comprised Venlafaxine hydrochloride in the form of mini-tablets or that the coating composition comprised a polymer and a water-soluble component. (*Id.* at 5.)

The Examiner found that Oosterbaan taught low water soluble salts of Venlafaxine, such as Venlafaxine maleate, in hydrogel-based extended release dosage forms including hard gelatin capsules comprising mini-tablets, pellets, beads, and/or spheres. (*Id.* at 5-7.) The Examiner also found that Oosterbaan taught that its tablets may be prepared according to any standard tableting technique, including by direct compression. (*Id.* at 6.) Additionally, the Examiner found that Oosterbaan taught that a preferred embodiment of its invention comprises mini-tablets. According to Oosterbaan, by using mini-tablets in a single capsule: (a) additive amounts of Venlafaxine may be provided without modifying the release profile; and (b) only one tablet formulation and shape is needed to produce multiple dosage strengths. (*Id.* at 7.) The Examiner found that Oosterbaan did not teach Venlafaxine hydrochloride as an active ingredient. (*Id.*) According to the Examiner Oosterbaan instead used Venlafaxine maleate to avoid irritations of Venlafaxine hydrochloride and aggressiveness of the hydrochloride on equipment. (*Id.*)

The Examiner found that Mulye taught compositions for coating a solid dosage form of medicament directed to a system for the controlled release formulation. (*Id.* at 8.) The Examiner also found that Mulye taught that its composition could be used to coat various cores that contain tablets,

spheroids, seeds, pellets, or other multi-particulate systems to provide for a controlled release of the active ingredient for longer than twenty-four hours. (*Id.*) Additionally, the Examiner found that Mulye taught that coating comprises a first component that is a water insoluble polymer and a second component that is a water soluble compound. (*Id.*) The Examiner also found that Mulye taught a method of preparing the coating by art recognized techniques, including dispersion of the polymer and water soluble compounds in a pharmaceutically acceptable solvent such as water. (*Id.* at 9.)

Additionally, the Examiner found that Mulye taught that its coating compositions had several advantages such as being safer by avoiding organic solvents, providing a water soluble component that is uniformly dispersed in the coat which allows uniform wetting of the coat and better uniformity of dry release between tablets, and allowing the rate of drug release to be controlled by controlling either the porosity or the thickness of the coat. (*Id.* at 9-10.) The Examiner found that Mulye taught a composition identical to that which is instantly claimed…. (*Id.* at 10.) The Examiner reasoned that since Mulye taught the instantly claimed coating composition, Mulye's composition inherently possessed the functional limitations of the coating of the claimed invention, i.e., the coating limits the initial rapid diffusion of the water-soluble drug substance from the functional core. (*Id.* at 11.)

According to the Examiner, the claimed pharmaceutical dosage form comprising an extended release formulation would have been obvious to a person of ordinary skill in the art at the time the invention was made over the combined teachings of the prior art. (*Id.* at 14.) Extended release dosage

forms comprising Venlafaxine hydrochloride formulated as spheroids filled into capsules was known, as taught by Sherman. (*Id.* at 14-15.) Dosage forms comprising mini-tablets of active ingredients, including Venlafaxine, filled into hard gelatin capsules were also known, as taught by Oosterbaan. (*Id.* at 15.) According to the Examiner, these teachings would have motivated a skilled artisan to formulate Sherman's controlled release Venlafaxine hydrochloride dosage form so that the capsules contain mini-tablets instead of spheroids because Oosterbaan taught that mini-tablets provide the advantage of being able to deliver multiple strength dosages by preparing just one form of the drug. (*Id.*)

The Examiner also found that coating tablets to control the release and delivery of drugs was known in the art, as taught by Mulye. (*Id.*) According to the Examiner, a skilled artisan would have been motivated to use Mulye's method of coating tablets when preparing the extended release formulation of Venlafaxine hydrochloride comprising a hard gelatin capsule containing mini-tablets as taught by the combination of Sherman and Oosterbaan to provide a controlled drug release formulation having the advantages of safety, reduced cost, uniformity of coating, and control features that Mulye disclosed. (*Id.*)

Appellants contend that since none of the cited prior art taught mini-tablets of the highly water soluble Venlafaxine HCL, the claimed invention would not have been obvious over the combination of references. (App. Br. 7.) According to Appellants, Sherman taught Venlafaxine HCL in the form of spheroids and not mini-tablets, Oosterbaan taught mini-tablets of low water-soluble Venlafaxine salts and not Venlafaxine HCL, and Mulye did not disclose mini-tablets or Venlafaxine HCL. (*Id.* at 5-6.)

Appellants also contend that Sherman and Oosterbaan taught away from producing mini-tablets of the extended release formulation of water-soluble Venlafaxine HCL. (*Id.* at 7.) According to Appellants, Sherman formulated Venlafaxine HCL as spheroids because "numerous attempts to produce extended release tablets proved to be fruitless" and that such formulation is difficult due to the high water solubility of the drug. (*Id.*) Appellants assert that "Oosterbaan took notice of the teachings of Sherman and deviated from using high water-soluble Venlafaxine HCl, as a person of ordinary skill would have done." (*Id.*) According to Appellants, "a person of ordinary skill cannot deduce that whatever process works for Venlafaxine salts would also work for Venlafaxine HCL, especially when there is evidence for the opposite." (*Id.* at 8.)

Appellants also contend that the cited prior art references do not teach the limitation that "each mini-tablet comprises a functional core and a functional coating layer or functional coating film, and wherein the functional core is produced with compression technology …." (*Id.*) Specifically, Appellants assert that: (a) Sherman taught producing spheroids via extrusion and spheronization; (b) Oosterbaan taught a hydrogel-based process, but did not provide any suggestion that the process would work with high water-soluble Venlafaxine HCL; and (c) Mulye did not disclose mini-tablets or Venlafaxine HCL. (*Id.* at 9.) Appellants assert, "[a]ccordingly, the combination … does not teach or make obvious the production of mini-tablets of an extended release formulation of the highly water soluble Venlafaxine HCL with compression technology." (*Id.*)

Additionally, Appellants assert that the suggested combination does not teach or suggest "a functional coating layer or functional coating film

that coats the functional core and limits the initial rapid diffusion of the water-soluble drug substance from the functional core." (*Id.*) According to Appellants, Mulye made "no reference to the problem or need to limit the initial rapid diffusion of the water-soluble Venlafaxine HCl from [the functional] core" nor suggested using the coating to do so. (*Id.* at 10-11.)

The issue is whether the record supports the Examiner's conclusion that the combined references would have made the claimed compositions prima facie obvious.

Findings of Fact

1. We agree with the Examiner's explicit findings regarding the scope and content of the prior art references (*see* Ans. 4-15).

2. Oosterbaan stated that "[a]lthough venlafaxine hydrochloride provides good pharmaceutical activity, it would be beneficial to find other forms of venlafaxine." (Oosterbaan col. 2, ll. 44-46.)

3. Oosterbaan stated that "venlafaxine forms that are easier [to] handle would be advantageous" and that it would be "desirable to provide a venlafaxine form that can be easily formulated into various dosage forms including hydrogel extended release tablets." (*Id.* at col. 2, ll. 46-54.)

Principles of Law

A prior art's disclosure does not constitute a teaching away where "such disclosure does not criticize, discredit, or otherwise discourage the solution claimed in the … application." *In re Fulton*, 391 F.3d 1195, 1201 (Fed. Cir. 2004). "[I]n a section 103 inquiry, 'the fact that a specific [embodiment] is taught to be preferred is not controlling, since all disclosures of the prior art, including unpreferred embodiments, must be

considered.'" *Merck & Co., Inc. v. Biocraft Laboratories*, Inc., 874 F.2d 804, 807 (Fed. Cir. 1989) (quoting *In re Lamberti*, 545 F.2d 747, 750 (C.C.P.A. 1976)).

The question of obviousness cannot be approached on the basis that an artisan having ordinary skill would have known only what was read in the references, because such artisan must be presumed to know something about the art apart from what the references disclose. *See In re Jacoby*, 309 F.2d 513, 516 (CCPA 1962). Moreover, the law presumes skill on the part of the artisan rather than the converse. *See In re Sovish*, 769 F.2d 738, 742-43 (Fed. Cir. 1985).

"Where, as here, the claimed and prior art products are identical or substantially identical…, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product." *In re Best,* 562 F.2d 1252, 1255 (CCPA 1977).

Analysis

After considering all the evidence and arguments, we conclude that the record supports a conclusion of prima facie obviousness. In particular, we are not persuaded of nonobviousness by Appellants' assertions that none of the cited prior art references taught mini-tablets of the highly water soluble Venlafaxine HCL. The Examiner relied on the combined teachings of Sherman and Oosterbaan as suggesting the formulation of Venlafaxine HCL using mini-tablets. (Ans. 14-15.) This combination merely involved substituting Sherman's spheroids with the mini-tablet form taught by Oosterbaan. (*Id.*)

Appellants assert that a skilled artisan would not have made this modification because Sherman and Oosterbaan allegedly taught away from producing mini-tablets of the extended release formulation of water-soluble Venlafaxine HCL. (App. Br. 7.) According to Appellants, Sherman and Oosterbaan avoided this formulation because "numerous attempts to produce extended release tablets proved to be fruitless" and that such formulation was difficult due to the high water solubility of the drug. (*Id.*) We disagree with Appellants' broad interpretation of these disclosures. The discussion in Sherman and Oosterbaan regarding "fruitless" attempts to produce extended release tablets of Venlafaxine HCL did not involve producing mini-tablets, coating mini-tablets, or encapsulating mini-tablets. (*See* Ans. 19). Consequently, as these references did not discourage or otherwise criticize a formulation including these characteristics, they cannot be said to have taught away from them. *See Fulton*, 391 F.3d 1195, 1201. Moreover, as the Examiner correctly explained, Oosterbaan did not disclose avoiding Venlafaxine HCL because it could not be formulated as an extended release mini-tablet. (Ans. 20.) Rather, Oosterbaan acknowledged that Venlafaxine HCL provided good pharmaceutical activity and disclosed that it would be advantageous to find other forms of Venlafaxine that are "easier to handle" and "can be easily formulated into various dosage forms including hydrogel extended release tablets." (FF-3.) Therefore, Oosterbaan's decision to use Venlafaxine maleate does not constitute a teaching away from using Venlafaxine HCL. *See Merck & Co., Inc.*, 874 F.2d at 807.

We are also not persuaded of nonobviousness by Appellants' assertion that none of the cited prior art taught that "each mini-tablet comprises a functional core and a functional coating layer or functional coating film, and

wherein the functional core is produced with compression technology ...." (App. Br. 8.) The Examiner found that Oosterbaan taught that its mini-tablets may be prepared according to any standard tableting technique, including by direct compression. (Ans. 6.) Appellants do not challenge this finding. Rather, Appellants assert that Oosterbaan only applied this process to low water-soluble Venlafaxine salts and therefore did not suggest that this process would work with high water-soluble Venlafaxine HCL. (App. Br. 9.) However, the question of obviousness cannot be approached on the basis that a skilled artisan at the time of the invention would have known only what was read in the references, because such artisan must be presumed to know something about the art apart from what the references disclose. *See Jacoby*, 309 F.2d at 516. Indeed, the law presumes skill on the part of the artisan. *See Sovish*, 769 F.2d at 742-43. Moreover, as discussed, Oosterbaan explained its decision to use low water-soluble Venlafaxine salts because these forms were "easier" to handle and formulate, not because they were the only forms to which its processing technique could be applied.

Appellants also contend that the Examiner's proposed combination does not teach or suggest "a functional coating layer or functional coating film that coats the functional core and limits the initial rapid diffusion of the water-soluble drug substance from the functional core." (App. Br. 10-11.) The Examiner found that "drug release from a coated sustained release composition is a functional limitation of the coating compositions...." (Ans. 11.) The Examiner also found that Mulye "explicitly" taught a coating composition "identical" to that of the claimed invention. (Ans. 10.) Appellants have not challenged these findings. According to the Examiner, since Mulye taught the claimed coating composition, Mulye's coating will

inherently possess the functional limitations of the coating of the claimed invention. (*Id.* at 11.) This reasoning is sound and supported by the facts. Appellants have not persuasively established otherwise, *see Best,* 562 F.2d at 1255, by merely asserting that Mulye made no reference to the problem. (App. Br. 10-11.)

Accordingly, we affirm the Examiner's obviousness rejections.

CONCLUSION OF LAW

The record supports the Examiner's conclusion that the combined references would have made the claimed compositions and methods prima facie obvious.

SUMMARY

We affirm the rejection of claims 1-23 under 35 U.S.C. § 103(a) as unpatentable over Sherman, Oosterbaan, and Mulye.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

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